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Cavotricuspid isthmus ablation among patients with persistent atrial fibrillation as a bridging therapy to maintain sinus rhythm — a pilot study

Ablacja cieśni trójdzielno-żylnej wśród pacjentów z przetrwałym migotaniem przedsionków jako terapia pomostowa służąca utrzymaniu rytmu zatokowego — badanie pilotażowe

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Abstract

Introduction. Among patients suffering from atrial fibrillation (AF), there is a certain population with episodes of typical atrial flutter (AFL). A detrimental effect of atrial remodelling caused by AF is well known, therefore duration of AF is an important prognostic issue for such patients. In our study we attempted an approach consisting of cavotricuspid isthmus (CTI) radiofrequency (RF) ablation and aldosterone receptor blocker administration for a purpose of maintaining sinus rhythm. The aim of this study was to assess long-term effects of such treatment in patients with AFL and/or AF.

Materials and methods. Population of 64 patients aged 64.7 years was divided into 3 groups: I — AFL (n = 34); II — AFL with paroxysmal AF (n = 13); III — persistent AF despite antiarrhythmic treatment (n = 17). CTI ablation was performed in all individuals, with subsequent direct current cardioversion in group III. Postablative antiarrhythmic medications were started in all patients in group II whilst in group III the current treatment was continued. Aldosterone receptor blocker was implemented in a part of group I and in all remaining patients. The mean follow-up period was 13.9 months.

Results. In group I, typical AFL recurrence occured in 3 patients (8.8%). In group II, 1 AFL recurrence was successfully treated with repeated ablation, and 1 AF relapse was noted. In group III, 7 AF relapses were treated definitely with pulmonary vein isolation or accepted as permanent AF. The primary success rate of the procedure was 91% vs. 85% vs. 59 % ($p < 0.05$).

Conclusions. CTI ablation is a therapeutic procedure for AFL and AFL concomitant with paroxysmal AF. Such procedure makes a moderately successful alternative for patients with persistent AF, while treatment with propafenone and aldosterone receptor blocker is provided. CTI ablation may constitute a bridging therapy aimed at preserving sinus rhythm in patients awaiting the pulmonary vein isolation.

Key words: atrial fibrillation, atrial flutter, cavotricuspid isthmus ablation, aldosterone receptor blocker, hybrid therapy

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Introduction

The coincidence of common atrial flutter (AFL) and atrial fibrillation (AF) is well known in clinical practice, however the interrelationship between them has not been fully understood. The 2016 ESC Guidelines on atrial fibrillation recommend to consider ablation of both arrhythmias as one therapeutic approach [1]. From a practical point of view, it should be emphasized that the experienced centres and operators have much too many patients waiting for the procedures to be performed and during this period some arrhythmias are considered to become permanent. Moreover, some circumstances may complicate performing the treatment and impede reaching a long-term success rate. Firstly, the type of AF (paroxysmal, persistent and long-standing persistent) affects an acute and long-term effect of pulmonary vein isolation (PVI). Recent data from a large STAR-AF II study presenting a comparison of three methods of persistent AF ablation (PVI alone, PVI plus ablation of complex fractionated electrograms or PVI plus lines in left atrium) shows 50–60% a success rate in the 18-month follow-up period [2]. There are several possible mechanisms of relatively low effectiveness of ablation in such patients. Multiple stressors, such as stretching of atrial myocardium, episodes of AF or other supraventricular arrhythmias, and renin–angiotensin–aldosterone system (RAAS) activation, are responsible for atrial remodelling and fibrosis. AF forms in the tissue self-perpetuating process facilitating the arrhythmia itself, the progression of electrophysiological and structural remodelling, and depleting successful therapeutic options. Despite the initial over-optimistic results of large trials pointing out that there is no difference in outcomes in the rhythm control group and the rate control one [3], in following summaries it was noted that restoration of sinus rhythm in an adequate fashion promotes lower mortality and morbidity. The approach presented in this paper is a modified hybrid therapy mentioned in the literature, that consists of radiofrequency (RF) ablation of cavotricuspid isthmus and pharmacological treatment.

The aim of this pilot study was to assess the middle-to-long-term efficacy of CTI ablation in patients with AFL/ /AF and AF.

Materials and methods

Sixty-four consecutive patients with typical AFL or AF who underwent radiofrequency catheter ablation were qualified to this study. Those with alone common-type AFL (n = 34, group I) received no anti-arrhythmic drug (AAD) therapy, before and after hospitalization. Group II consisted of 13 patients with AFL who either had concomitant paroxysmal AF or who suffered from paroxysmal AF during the ablation procedure. Patients with persistent AF despite previous appropriate AAD therapy in medical records (n = 17) constituted a Group III. AAD, mostly propafenone, were administered by referring cardiologists. Group III patients were treated with direct current cardioversion during the RF ablation procedure with subsequent assessment of CTI block and additional energy application if necessary. Post-procedural AAD was administered in group II whilst in group III the current treatment was continued.

We performed an initial clinical evaluation that included past medical history, physical examination, 12-lead surface electrocardiogram (ECG), blood chemistry tests and transthoracic echocardiography with colour flow Doppler measurements prior to the procedure in all of the patients. Oral anticoagulation was prescribed according to CHA_2DS_2VASc risk score. The use of medications, including beta-adrenolytics, AAD, angiotensin-converting enzyme inhibitors, was determined at the discretion of the responsible clinician. This study was carried out in accordance with the Principles of the Declaration of Helsinki (1975) and approved by the local Ethical Committee. All enrolled patients gave their written informed consent.

Performed RF ablations were aimed at acquiring cavotricuspid isthmus bidirectional block, assessed after 20 minutes of observation. A standard diagnostic quadripolar electrode (Boston Scientific, Boston, MA, USA) was placed in the coronary sinus, and afterwards 8 mm ablative catheter (Bard Electrophysiology, C.R. Bard, Lowell, MA, USA or Boston Scientific, Boston, MA, USA) or mini electrode-tipped (IntellaTip MiFi XP, Boston Scientific, Boston, MA, USA) were located under fluoroscopy at CTI area. The standard procedure of EPS was performed in patients with AFL prior to ablation. CTI-dependence of circulatory wave was proved by entrainment pacing. Bidirectional isthmus block was confirmed by pacing from the coronary sinus ostium and the low lateral right atrium in the presence of double potentials. Group III patients with initial AF were treated with direct current cardioversion (DCC) (300–360 J) after initial application of RF energy, with further assessment of ablation line and additional RF application if needed. After DCC, patients were monitored at intensive cardiac care unit. The follow-up was performed at outpatient clinic or at referring cardiologists, and consisted of taking medical history towards symptoms of arrhythmia, echocardiography and ECG-Holter monitoring.

The study protocol was approved by local Bioethics Committee — KB-166/2017.

The results were presented as means and standard deviations or percentages, as appropriate, and were compared using multi-variate analysis (1-way ANOVA). Calculations were performed using the STATISTICA v12.0 statistical package, where $p < 0.05$ was considered as statistically significant.

Results

Clinical characteristics of enrolled population are presented in Table 1. These parameters were perfectly matched

Table 1. Baseline patients' clinical characteristics

Parameter	Group I (n = 34)	Group II (n = 13)	Group III (n = 17)	p value
Women	20 (58.8%)	7 (53.8%)	11 (64.7%)	NS
EHRA score	2.3 ± 0.7	2.4 ± 0.7	2.2 ± 0.8	NS
Hypertension	20 (58.8%)	6 (46.1%)	8 (57.1%)	NS
CAD	2 (5.9%)	2 (15.4%)	2 (11.8%)	NS
Heart failure	1 (3%)	0	1 (7.1%)	NS
Diabetes mellitus	10 (29.4%)	2 (15.4%)	2 (14.3%)	NS
Stroke	5 (14.7%)	2 (15.4%)	3 (21.4%)	NS
Medications:				
• beta-adrenolytics	25 (73.5%)	9 (69%)	11 (78.5%)	NS
• CCB	5 (14.7%)	1 (7.7%)	1 (7.1%)	NS
• ACEI or ARB	13 (38.2%)	3 (23%)	5 (35.7%)	NS

NS — non-significant; EHRA score — EHRA classification of arrhythmia symptoms; CAD — coronary artery disease; CCB — calcium channel blocker; ACEI — angiotensin-converting enzyme inhibitor; ARB — angiotensin receptor blocker

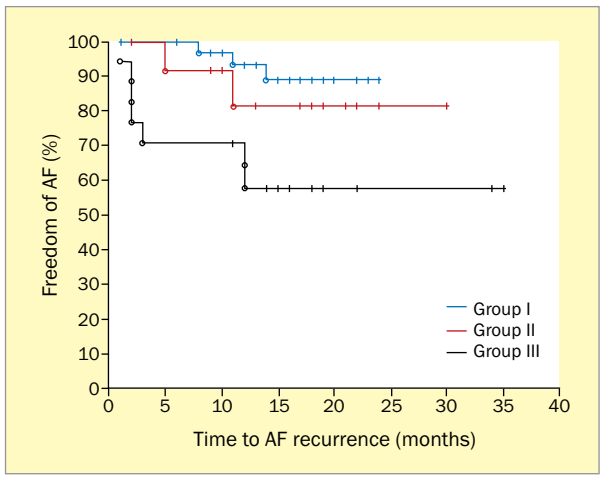

Figure 1. Kaplan-Meier plot of arrhythmia-free survival; AF — atrial fibrillation

for 3 groups (with no statistically significant differences among them). Periprocedural parameters were measured, including the number of RF applications, total ablation time, mean temperature, mean impedance, and mean power during the applications. These results were also similar among all groups, and listed in Table 2. Arrhythmia-free survival among the studied patients was shown using the Kaplan-Meier survival curves (Fig. 1).

In group I the AFL recurrence was present in 3 patients (8.8%) and was successfully terminated in all 3 patients (8, 11 and 14 months). No AF was observed during the follow-up. In Group II there was 1 AFL recurrence (after 5 months) treated successfully with repeated ablation, and 1 AF episode treated with propafenone with signs of sinus node dysfunction and a subsequent pacemaker implantation (11 months atrial pacing without arrhythmia episodes). In group III, 7 AF relapses were treated definitely with pulmonary veins isolation or accepted as permanent AF.

Discussion

It has been shown that administration of Class Ic AAD can transform AF into AFL. Class Ic AAD causes slowing conduction, prolongation of the atrial refractory period and decrease excitability of myocardium. Thus, it may promote forming larger re-entry loops (flutter wave) rather than smaller circuits (fibrillation activity). However, the clinical and electrophysiological background underlying the organization of AF into AFL during antiarrhythmic therapy is not fully proved [4, 5]. Such evolution was reported in the early 1990s in up to 20% of patients receiving Ic AAD treatment (so-called Ic AAD-AFL) [6]. Hence, providing the beta-adrenolytic treatment in order to avoid 1:1 conduction was necessary. Some studies were performed on that basis [4, 7, 8] and reported that among patients suffering from refractory AF, who develop Ic AAD-AFL after a successful CTI ablation, AF recurrences were reduced.

Radiofrequency ablation of CTI was constantly considered as elimination of one of the possible factors driving AF. The concept was based on hypothesis that in some patients AF is facilitated and/or perpetuated by a re-entry loop circulating through CTI. This re-entrant activation can be conducted to the left atrium by the Bachmann's bundle or the coronary sinus. The most interesting issue is its efficacy in populations suffering from AFL concomitant with paroxysmal, or even more important, persistent AF. Such approach was reported in a few papers. The mean follow-up time was different in those studies. Reithmann et al. conducted an observation of 46 patients with

Table 2. Ablation characteristics acquired from LabSystem Pro™, reported as mean ± standard deviation

Parameter	Group I (n = 34)	Group II (n = 13)	Group III (n = 17)	p value
Number of RF applications	21.3 ± 10.9	24.6 ± 9.9	25.5 ± 8.4	p = 0.51 NS
Total ablation time (min)	13.7 ± 7.17	18.4 ± 8.14	16.8 ± 6.83	p = 0.37 NS
Temperature [°C]	50.9 ± 5	50.1 ± 4.6	53.7 ± 4.9	p = 0.17 NS
Impedance [Ω]	82.5 ± 12	82.6 ± 29	77.8 ± 10.7	p = 0.74 NS
Power [W]	35.5 ± 15.3	35.7 ± 18.8	30.0 ± 16.8	p = 0.63 NS

RF — radiofrequency; NS — non-significant

paroxysmal and persistent AF who developed AAD-AFL after administration of amiodarone, flecainide, propafenone and sotalol, respectively [8]. After successful CTI ablation, previously administered AAD were continued. The recurrence rate of AF in a mean 21-month post-ablation period was 33%, irrespective of the initial antiarrhythmic treatment. Huang et al. reported an AF recurrence rate of 11% in an AAD-AFl population who underwent CTI ablation, in a 14-month follow-up [10]. More recently, Schmieder et al. [11] showed an observation comparing occurrence of AF before and after CTI ablation due to AFL. After mean 16.3-month observation there was a significant reduction of AF incidence (112 patients, 33%) with reference to the preablation period (198 patients, 55%, $p < 0.001$). Anastasio et al. reported AF relapse rate after such intervention as high as 90.3% in investigated group which completed a 5-year follow-up [12].

In 2014 García Seara et al. published a paper [13] that contained a recent analysis of a treatment of 3 populations: the first one including AAD-AFL patients, the second — with previous coexistence of AF and AFL, and the third with AFL alone. We should highly appreciate both the over 10-year follow-up period, that is rarely observed in this therapeutic approach, and the size of populations enrolled. Results have shown high incident rates, similar among AAD-AFL and AFL diagnosed prior to AF. Nevertheless, to our minds, the emphasis on following the AAD therapy was insufficient.

Multiple stressors, such as stretching of atrial myocardium, episodes of AF and other supraventricular arrhythmias, and RAAS activation as well, may favour propagation of AF [14, 15]. For instance, molecular and histological effects of high aldosterone activity were evaluated in several studies. High expression of mineralocorticoid receptors frequently observed during AF caused atrial ionic remodelling [16], which was further attenuated by spironolactone. Animal in vivo model of injected aldosterone resulted in anisotropy of atrial conduction, recorded in a epicardial stimulation map [17]. Furthermore, registered conduction abnormalities were associated with structural remodelling represented by atrial fibrosis and hypertrophy, thus being responsible for forming a substrate for atrial arrhythmias.

Some clinical studies, including double-blind randomized trials, were conducted to assess influence of aldosterone receptor blockers in preventing recurrences of AF. Spironolactone, as it was evaluated with regards to safety and efficacy in patients with structural heart diseases, seems to be an attractive alternative, or an additional drug, for treating AF. Treatment with spironolactone combined with beta-adrenolytic was successful in reducing AF burden and the number of AF-related hospitalizations irrespective of structural heart disease [17, 18]. Recently published meta-analysis concerning RAAS blockade with a cumulative number of 5332 patients showed a lower risk of new-onset AF and recurrent AF as well. Reduction was even more prominent among patients without a previous diagnosis of heart failure [20].

Restoring and maintenance of the sinus rhythm may cut the vicious circle of adverse atrial remodelling caused by AF. Thus, our goal was to maintain the sinus rhythm in such population until a definitive ablation of this arrhythmia. Speaking of perspectives for ablation of AF in Poland, we must not forget about 30 procedures per million inhabitants per year — one of the lowest rates in the Central Europe. Hence, availability of PVI in Polish reference centres is still insufficient, with awaiting times as long as 1 year being reported [21] and our clinical experience suggesting awaiting times up to 2–3 years in highly experienced facilities. This study possesses limitations as a retrospective one, due to relatively low number of participants and the possibility of hidden, asymptomatic recurrences of AF that may not have been detected. Therefore there is a space for long-lasting ECG monitoring, according to latest guidelines published by Baranowski et al. on behalf of Polish Cardiac Society.

Aforementioned paper recommends to search for recurrences of arrhythmia in patients maintaining sinus rhythm after ablation [22].

Conclusions

In our study, we found that CTI ablation is a curative procedure for patients with typical AFL and paroxysmal AF with coexistent AFL. Such approach, provided that antiarrhythmic and spironolactone medications are used, is a moderately successful treatment for patients with persistent AF. Presented results should be confirmed in a prospective fashion.

Conflict of interest(s)

Authors declared no conflict of interest(s).

Streszczenie

Wstęp. W znacznej części populacji pacjentów z migotaniem przedsionków (AF) współistnieją napady trzepotania przedsionków (AFL). Zważywszy na niekorzystny efekt AF w postaci remodelingu przedsionka, istotne dla rokowania pacjentów jest, by okres arytmii był jak najkrótszy. W opisanym niżej badaniu, w celu uzyskania rytmu zatokowego, podjęto próbę leczenia ablacją prądem o częstotliwości radiowej (RF) cieśni trójdzielno-żylnej (CTI) oraz antagonistą receptora aldosteronowego. Celem badania była ocena wyników odległych takiego postępowania u chorych z AFL i/lub AF poddanych ablacji CTI.

Materiał i metody. Badana populacja składała się z 64 pacjentów (średni wiek 64,7 roku) podzielonych na 3 grupy: I — AFL (n = 34); II — AFL z napadami AF w wywiadzie (n = 13); III — przetrwałe AF mimo leczenia antyarytmicznego (n = 17). Ablację CTI przeprowadzono u wszystkich pacjentów. Pozabiegowe leczenie antyarytmiczne w grupie II rozpoczęto u wszystkich chorych, a w grupie III kontynuowano dotychczasowe leczenie. Antagonistę receptora aldosteronowego zastosowano u części pacjentów z grupy I oraz u wszystkich z pozostałych grup. Okres obserwacji wynosił średnio 13,9 miesiąca.

Wyniki. U chorych z grupy I nawrót AFL obserwowano u 3 pacjentów (8,8%), u których wykonano kolejny zabieg, po którym nie notowano AF/AFL podczas obserwacji. W grupie II doszło do jednego nawrotu AFL w ciągu 5 miesięcy, poddanego ponownej ablacji zakończonej sukcesem, oraz jednego epizodu AF (11 miesięcy bez nawrotu arytmii). W grupie III zanotowano 7 nawrotów AF, z następczym zabiegiem izolacji żył płucnych lub uznanych za utrwalone AF. Odsetek skutecznych pierwotnych zabiegów w okresie obserwacji wyniósł 91% w porównaniu z 85% w porównaniu z 59% ($p < 0,05$).

Wnioski. Ablacja CTI stanowi procedurę terapeutyczną dla chorych z typowym AFL oraz osób z AFL i towarzyszącym napadowym AF. Zabieg ten jest umiarkowanie korzystnym rozwiązaniem u pacjentów z przetrwałym AF, pod warunkiem zapewnienia leczenia antyarytmicznego propafenonem i antagonistą receptora aldosteronowego. Ablacja CTI może się okazać terapią pomostową w przetrwałym AF przed izolacją żył płucnych służącą utrzymaniu rytmu zatokowego.

Słowa kluczowe: migotanie przedsionków, trzepotanie przedsionków, ablacja cieśni trójdzielno-żylnej, antagonista receptora aldosteronowego, leczenie hybrydowe

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